Review article: The effect of borax as a food additive on energy metabolism

by Dr. Damat

Review article: The effect of borax as a food additive on energy metabolism

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Abstract:

Borax is still widely used for food in the community. Borax can attack mitochondria and cytoplasm where cellular energy metabolism occurs. The purpose of this study was to analyze the impact of borax on energy metabolism. Settings and Design of this study used Review article. The writing method was based on scientific phenomena that occurred in the research which was then analyzed deeply based on theories taken from the scientific literature. The Result of this study**,** Boron ions affect the activity of at least 26 different enzymes that are needed for energy metabolism. Boric acid as active substances of borax can form stable complexes with hydroxyl compounds from glucose, protein and fat which are the raw materials for energy metabolism, and inhibit nicotinamide adenine dinucleotide (NAD^+) activity which is a coenzyme in energy metabolism. Decrease in adenosine triphosphate (ATP) due to boric acid through the binding of NAD^+ and an increase in thermogenic protein pathways. The ATP reduction which disrupts ion pumps and accumulation of boron ions will damage the composition of ions in the cytoplasm where the process of glycolysis occurs. This ion pump disruption will also cause cell swelling, and disrupt the balance of ions which will lead to mitochondrial dysfunction and damage (the site of the Krebs cycle and oxidative phosphorylation). Conclusions of this study, Borax has a negative effect on energy metabolism, through the macronutrient, NAD^+, enzymes, ATP, cytoplasm and mitochondria pathway.

Keywords: Cycle of energy, dangerous chemical, Sodium tetraborate decahydrate.

How to cite this article: Pratiwi, *et al*. (2020): Review article: The effect of borax as a food additive on energy metabolism, Ann Trop & Public Health;23 (S8): 1317–1323.

DOI: http://doi.org/10.36295/ASRO.2020.23819

Introduction

Borax or sodium tetraborate decahydrate is a type of sodium salt that is widely used as a non–food grade additive in Indonesian society. Based on the Joint Regulation of the Minister of Home Affairs and Head of the Drug and Food Supervisory Agency, Republic of Indonesia, No. 43 of 2013 and No. 2 of 2013, Chapter II, Article 3, concerning "supervision of hazardous substances which are misused in food", borax is included as a dangerous chemical which its use must be monitored in the community [(1)]. However, although it has been prohibited from use in food, there are still many food vendors, especially snacks for school children, who still use borax for food additives. The results of the PJAS – *Pengawasan Pangan Jajanan Anak Sekolah* (Supervision of School Children Food Snacks) by the BPOM – *Badan Pengawas Obat dan Makanan* (Food and Drug Supervisory Agency) until 2013 and 2014, showed that snacks for school children who did not meet health requirements were around 19.21 % and 23.82 %, due to abuse of hazardous substances (materials prohibited from being used for food such as borax, formalin, rhodamine B coloring agent and methanyl yellow) and microbial contamination or food additives that exceed the limit (such as cyclamate and benzoate) [(1)]. While The Food Safety Survey in 1 504 IRTP – *Industri Rumah Tangga Pangan* (Food Home Industries) in 18 provinces showed that there were misuse of hazardous materials, such as formalin (4.89 %), borax (8.80 %) and rhodamine B and methanyl yellow (4.89 %), on IRTP products [(2)]. The data shows that borax is still used for food and tends to be relatively the most common compared to formaldehyde and other quality requirements in the community. The negative effects of borax use on health, for example, at high doses in the body, will cause symptoms of dizziness, vomiting, diarrhea, abdominal cramps, low blood pressure, anemia, fever and other internal organ damage, including the brain, even death. In addition, the residue left behind can cause a systemic impact on the body. Its visible effect from the outside is the hardening of the skin and the death of the outer tissue of the skin. More dangerous effects include damage to the liver, stomach, small intestine, large intestine, testicular and ovarian organ infertility, and stimulate the growth of cancer cells. Borax attacks cells, especially in the mitochondria, and accumulates in the cytoplasm, which disrupts cell metabolism [3]. Cytoplasm and mitochondria are cellular organelles which play a major role in energy metabolism. The mechanism of borax in the human body in influencing energy metabolism is not yet known. Therefore, based on the impact that occurs at the cellular level, specifically the cytoplasm and mitochondria, it is necessary to conduct an initial study in the form of a literature review on the effect of using borax as a food additive on energy metabolism. The purpose of this study was to analyze the impact of borax which is used as a food additive on energy metabolism. The special purpose is describing the use of borax as a non–food grade additive, analyzing the impact of borax on energy metabolism, analyzing further consequences which would be expected if the energy metabolism process was disrupted, and described solutions that can be done to overcome problems that arise. This study is useful to develop a theory about the impact of borax which is used as a non–food grade additive to energy metabolism which will inhibit the growth and development of school children. In addition, the results of this study provide opportunities for theoretical development of other non–food grade chemicals' effects on energy metabolism in particular and other types of metabolism in general. Practically, this study provides information to the public about the potential of borax which can affect the body's energy metabolism, which will have broad implications for the health of the body.

Materials and methods

The method of the writing of this article was based on scientific phenomena that occurred in studies conducted by the author in private from September to July 2015 [4], which was then analyzed more deeply based on a study of theories about borax and energy metabolism and their relationship each other taken from various research journals and textbooks. The references were strictly examined on 15 yr at the oldest, and reflected in Google and Google Scholar.

Discussion

Use of borax as a non–food grade additive:

Food additives are widely used by street food producers that are sold in schools and on the roadside by street vendors, so that they can be consumed easily and cheaply by the community, especially elementary to high school children [5]. The results of Supervision of School Children Food Snacks (PJAS) by the POM until 2013 and 2014 showed that snacks for school children who did not meet health requirements were around 19.21 % and 23.82 % for misusing hazardous materials (materials that are prohibited from being used for food such as borax, formalin, rhodamine B coloring agent and methanyl yellow) and microbial contamination or food additives that exceed the limit (such as cyclamate and benzoate) [1]. The annual report of the Food and Drug Supervisory Agency (BPOM) reported that testing of food products circulating in the community that had received some food including foods that did not meet the requirements was because of containing dangerous food additives which were prohibited from being used, such as formalin and borax. The test was carried out on 4 635 food samples and found as many as 170 samples (3.67 %) of food containing borax. The food samples were grass jelly, red *candil*, seaweed, *dawet*, *dawet*, meatballs, *batagor*, *siomay*, rice cake, *empek–empek*, noodles, brains, tofu and crackers [6]. Testing of borax has also been carried out on several types of food products in Padang, Indonesia. The tests conducted by Ervin on meatball samples sold around Jati and Jati Baru Villages, Padang City, Indonesia in 2016, found that 11 out of 18 samples tested positive for borax [7]. The use of borax in crackers products turns out to be quite a lot and common. Research on borax content in crackers carried out on 12 samples of crackers circulating in Traditional Markets, Semolowaru, Surabaya, Indonesia showed that all positive samples contained borax. So did the results of quantitative borax analysis using a UV–vis spectrometer. Borax content in the sample ranged from 11.80 mg L^{-1} to 119.90 mg L^{-1} with the lowest level in "Uyel" crackers which was 11.80 mg L^{-1} and the highest borax content in "Puli Galar" crackers which was 119.90 mg L^{-1} [8].

Effect of borax on general energy metabolism:

Energy metabolism is the overall reaction that occurs in cells, including the process of decomposition and synthesis of chemical molecules that produce and require heat (energy) and catalyxed by enzymes. In this case the metabolism includes: i) The synthesis pathway (anabolism or endorgenic), which combines small molecules into more complex macromolecules; requires energy supplied from ATP hydrolysis, ii) Degradative pathways (catabolism or genetics), which break down complex molecules into simpler molecules; reeasing the energy needed to synthesis ATP [9]. Based on oxygen requirements, there are two kinds of metabolism, namely aerobic and anaerobic metabolism. in its reaction, catabolic aerobic metabolism goes through several stages, the glycolysis stage, the citric acid cycle stage (the krebs cycle), and the stage of oxidative phosphorylation (electron transport chain). The three stages are presented in figure 1.

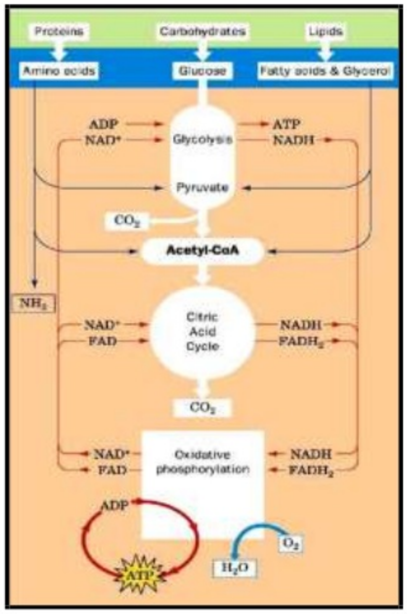

Figure 1: The process of catabolic aerobic energy metabolism

Figure 1 shows that protein, carbohydrates and fats are raw materials which, when metabolized, produce energy. The NAD^+ and FAD are coenzymes of the process of energy metabolism. Energy is produced in the form of ATP chemical compounds, while the process of energy metabolism occurs in the cytoplasm (glycolysis) [(10)] and mitochondria (krebs cycle and oxidative phosphorylation) [(11)]. In a study, boric acid at high doses (3.375 mmol B kg^{-1} bw and 4.5 mmol B kg^{-1} bw) caused changes in energy metabolism in type IIB muscle fibers, and was influenced also by exposure time [(12)]. Changes that occurred were measured based on a decrease in ATP and glucose which was the output and raw material of energy metabolism. The study showed that energy protection in broiler muscles against boric acid toxicity would be the most important subject of study.

Borax effect on components of energy metabolism:

Macronutrients (protein, carbohydrates and fats)

The effect of borax on the components of energy metabolism is certainly influenced by the potential physical and chemical properties of borax, the metalloid boron (B) nature as the main component, and its effect on many enzymes and minerals [(13)]. Boric acid can form complexes with various biomolecules, such as glucose, protein and fat [(14)]. These compounds will form stable complexes with hydroxyl compounds such as carbohydrate components [(15)]. In another study, boric acid caused a decrease in the concentration of metabolism such as glucose, glycogen and lactate, due to the formation of complexes between boron and hydroxyl compounds [(16)]. The reaction between boron and hydroxyl groups is presented in figure 2.

Figure 2: Interaction of boric acid with sugar vicinal diol [(17)]

The study of the effect of acute boric acid doses on chicken breast muscle energy metabolism found that administration of boric acid at a dose of 3.375 mmol B kg^{-1} bw (for 24 h) and 4.5 mmol B kg^{-1} bw (for 24 h and 48 h) caused decreased concentration of metabolites (glucose, glycogen, lactate) in muscle fibers (type IIB) in broilers [(12)]. The reduction in glucose in the culture medium is caused by boronglucose interactions. Similarly, the formation of the glucose–boron complex in vivo results in a decrease in the energy substrate in cartilage cells [(18)].Carbohydrates, proteins and fats are organic nutrients or macronutrients which are the main ingredients for producing energy for the body. Therefore, energy metabolism is expected to experience a decrease in raw materials due to boron bonding with the organic nutrient hydroxyl group. In the end the production of energy (ATP) produced also decreased.

NAD^+ (nicotinamide adenine dinucleotide)

Borate is able to inhibit activity of nicotinamide adenine dinucleotide (NAD^+) [(19)]. In the process of oxidative phosphorylation which produces ATP, NAD^+ which is a coenzyme, acts as an electron carrier from one organic component to another organic component [(20)]. Therefore, inhibition of NAD^+ by borax is thought to inhibit and decrease ATP synthesis. In addition, hydroxyl groups from NAD are known to form complexes with borate compounds [(21)]. Boron with adjacent hydroxyl groups (transferase) has a tendency to form complexes with organic molecules, and is thought to have interactions with important biological substances containing polysaccharides, pyridoxine, riboflavin, dehydroaskorbic acid, and pyridine nucleotides [(22)]. Boron binds strongly to furanoidcis–diols, which include erythritan, ribose, and apiose. Apiose is present in all vascular cell walls [(23, 24)]. Nicotinamide adenine dinucleotide (NAD^+) and nicotinamideadenine dinucleotide phosphate (NADP) contain a ribose component that is active in energy metabolism. Binding them means affecting the processes of certain metabolic pathways [(24)]. It was reported that NAD^+ is an important cofactor for the five sub–classes of oxidoreductase enzymes and has strong relevance for boron. The typical chemical structure of boron allows it to react with many other metabolites and enzymes, and is thought to be able to modify mineral metabolism and energy in humans and animals [(25)].

ATP (adenosine triphosphate)

Adenosine triphosphate (ATP) is a complex organic chemical that provides energy to drive many processes in living cells, such as muscle contraction, nerve impulse propagation, and chemical synthesis. Found in all life forms, ATP is often referred to as a "molecular currency unit" of intracellular energy transfer [(26)]. The study of the determination of LC_{50} Borax ($Na_2O_2B_2O_3.10H_2O$) in Tenebrio mollitor (*Coleoptera tenebrionidae*) and determination of sublethal borax dose toxic effects on Mealworm larvae, it was found that the higher the borax dose given to 3 000 mg L^{-1}, the lower the larval weight. This can be explained by the theory of energy use, where as a result of the stress caused by the use of borax in pesticides, there is a decrease in the level of ATP or suppression of the engine of energy production [(27)]. In a study of the mechanism of weight loss, the intake of oral boric acid is thought to cause over–expression of thermogenic proteins in adipose tissue and skeletons. Increased thermogenesis through the UCP protein pathway (Uncoupling protein, ie the main protein in thermogenesis and regulation of energy expenditure mechanisms) results in accelerated lipolysis and weight loss [(28)]. The UCP_1 type is involved in terminating proton transport from ATP synthesis, because it increases the demand for fuel substrates, such as glucose and lipids in the process of oxidative phosphorylation [(29)]. Whereas, UCP_2 and UCP_3, similar to UCP_1, can reduce protons electrochemical gradients across the mitochondrial membrane which cause a decrease in ATP production when overexpressed in mammalian cells [(29)]. The effect of weight loss is indicated by UCP_1 and UCP_2 overexpression. Obesity is characterized by an imbalance between energy intake and expenditure [(28)]. Administration of boric acid at a dose of 3.375 mmol B kg^{-1} bw (for 24 h) and 4.5 mmol B kg^{-1} bw (for 24 h and 48 h) caused a decrease in ATP metabolite concentration in muscle fiber (type IIB) in broilers [(12)].

Cytoplasm

Cytoplasm is a component of cells surrounded by cell membranes. Cytosol is a component of the cytoplasm. Cytoplasm consists of cytosol, organelles, and cytoplasmic inclusions. Organelles in the cytoplasm include the nucleus, mitochondria, golgi apparatus, endoplasmmic reticulum, lysosomes and, in plant cells, vacuoles and chloroplasts. Some insoluble particles suspended in the cytoplasm are called cytoplasmic inclusions [(30)]. Boron levels in male rat tissues on 7 d after exposure to boric acid 9 000 mg L^{-1} (1 575 mg L^{-1} boron) in food (g boron every g tissue), sequentially from the highest to lowest, were bones, seminal vehicle, adrenals, seminals vehicle fluid, kidney, epididymis, testis, plasma (cytoplasm), large intestine, prostate, hypothalamus, muscle, brain, liver and adipose [(31)]. As a result of borax administration, there is a decrease in ATP which will affect the work of Sodium (Na^+) and Potassium (K^+) pumps (Na^+/K^+ –ATPase or sodium–potassium adenosine triphosphatase or known as sodium–potassium pump), to pump ions Na^+ out of the cells (efflux) and K^+ ions into the cell (influx). The disrupted Na and K pumps will cause ion imbalances in the cell which results in an increase in Na^+ ions and Ca^{2+} ions, including the accumulation of Boron ions, in the cytoplasm. The imbalance of ion content that occurs in the cytoplasm is thought to interfere with the process of glycolysis (the stage of energy metabolism) (4). Finally, the process of energy metabolism in general will be disrupted.

Mitochondria

Mitochondria are cellular organelles that serve as factories where energy is produced for living things. Mitochondria play an important role in cellular metabolism and, in different locations, can adapt to reflecting diverse metabolic demands on different cell regions (16). Boric acid causes damage to several parts of the mitochondria. Lack of ATP metabolites and metabolic damage in mitochondria is dangerous for cell survival and function, especially tissues that are highly dependent on energy, such as skeletal muscle (16). It is well known that energy production to support muscle contraction in cells mostly originates from mitochondria (32). Therefore, it is suspected that mitochondrial damage is the cause of reduced ATP production. Research on the effect of acute boric acid dose on energy metabolism of broiler breast muscles proves that boric acid administration at a dose of 3.375 mmol B kg^{-1} bw (for 24 h) and 4.5 mmol B kg^{-1} bw (for 24 and 48 h) caused damage to subsarcolemmal and intermyofibrillar mitochondria (crystalline dissolution), which was also observed as a toxic effect of boric acid (4.5 mmol B kg^{-1} bw). As a result, the administration of boric acid at these doses is quite dangerous for energy metabolism in muscles (12). The theoretical study in Pratiwi's research showed that the decrease in the amount of ATP production in mitochondria affected the work of Sodium (Na^+) and Potassium (K^+) pumps (Na^+/K^+ ATPase or sodium–potassium adenosine triphosphatase or known as sodiumpotassium pump) to pump Na^+ ions out of the cells (efflux) and K^+ ions into the cells (influx) (4). Disrupted Na and K pumps will cause ion imbalance in the cell, which results in an increase in Na^+ ions and Ca^{2+} ions in the cytoplasm. Increased Na^+ and Ca^{2+} ions in the cytoplasm induce an increase in Ca^{2+} ions in mitochondria which results in a decreased mitochondrial membrane potential. This will disrupt the balance of Ca^{2+} and inhibit ATP synthesis in mitochondria, which has implications for mitochondrial dysfunction. In the end, if the above phenomenon continues to occur and accumulates, the mitochondria will be damaged.

Possible effects of disruption of energy metabolic processes:

The administration of borax affects the energy metabolism of male mice which is characterized by a decrease in ATP meta–bolites which results in systemic disorders. Systemic disorders are thought to affect the work of sodium (Na+) and Potassium (K^+) ions. This will cause failure of membrane transport of Na^+ and K^+ ions by the Na^+/K^+–ATPase ion pump which causes the sodium to enter the cell, while potassium goes out of the cell. This condition is also sometimes followed by an increase in Ca^{2+} influx, in addition to the release of Ca^{2+} from intracellular deposits. With the increase in ion levels in cells, the osmotic pressure in cells is greater than outside the cell, so that H_2O in the cell will increase. The increase in H_2O in cells that is continuous and long due to exposure to borax is thought to cause the cells swollen and will cause dilatation of endoplasmic reticulum. As a result, there is a decrease in mitochondrial function and increased permeability of intracellular membranes. If the cell gets swollen, the cell will eventually break or become seriously damaged, which is an indication of the occurrence of necrosis. In the end, this condition can cause damage to organs (especially the liver and kidneys, the main organs of chemical metabolism) (33).

Solution to prevent problems due to the use of borax in food:

To prevent further damage due to the use of borax in food, one needs to consume herbs that are rich in flavonoids that can protect levels of NAD^+ (Nicotinamide Adenine Dinucleotide) in cells (33), to consume Vitamin B complex (specifically Vitamin B3, nicotinamide and nicotinic acid) which are biosynthetically converted into nicotinamide adenine dinucleotide, to maintain NAD^+ levels in the cells. In addition, the community needs to be educated about the characteristics of foods that contain borax and how to detect the presence of borax in food easily and affordably, for example by using turmeric method. The aim is is to increase public (consumers and producers) awareness independently of food security.

Conclusions

Borax is still widely used for food (such as grass jelly, red *candil*, seaweed, *dawet, bakwan*, meatballs, *batagor*, *siomay, lontong, empek–empek,* noodles, brains, tofu and crackers) in the community. Borax has a negative impact on energy metabolism through the following pathways: Formation of bonds with hydroxyl groups in raw materials (carbohydrates, proteins and fats) energy metabolism, binding of hydroxyl groups NAD^+, thus inhibiting the activity of NAD^+ which is a coenzyme of energy metabolism, boron affects activities of at least 26 different enzymes, most of which are needed for energy substrate metabolism, for example oxidureductase; decreased energy production (ATP), damages the ion composition in the cytoplasm, which is the location of glycolysis (energy metabolism stage) in cells; and damages energy plants in in cells or mitochondria. The continued effect of borax on energy metabolism is the damage to cells and organs. The solution to prevent further damage is to consume herbal sources of flavonoids, Vitamin B_3, and provide counseling to the community to increase awareness independently of food security.

The Authors advise the government to strictly and continuously control the use of borax and other non–food grade additives. Clear legal sanctions need to be given for violations of the use of non–food grade additives in food. Academics must be diligent and systematic in carrying out criticism and research on food safety issues in the community. Communities need to be given information about the characteristics of foods that use borax or other non–food grade additives, and about negative consequences when those additives are used in food, so that it will increase knowledge and awareness of the community.

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